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Application No. 10/781,503

AMENDMENTS TO THE SPECIFICATIONIn the Specification

Please substitute the following amended paragraph(s) and/or section(s) (deleted matter is shown by strikethrough and added matter is shown by underlining):

At page 11, lines 10-24, please replace the paragraph with the following.

Devices used in cardiology procedures include, for example, distal protection devices to prevent ischemic event associated with embolus. Physicians also use a variety of medical devices to correct problems associated with the cardiovascular/vascular system, urinary tract, the neurological system, orthopedic elements, etc. While in principle SCF fibers can be used in any of the medical devices described above, a few medical devices are of particular interest. Such devices of particular interest include, for example, embolic protection devices, vascular closure devices, aneurysm repair device, catheters, artificial livers, artificial heart muscle, drug delivery devices, synthetic nerves, biological adhesive attachment structures, and orthopedic components, such as tendon repair devices. Suitable embodiments of embolism protection devices are described further in copending U.S. Patent Application serial number 10/414,909 now U.S. patent 7,303,575 to Ogle, entitled "Embolism Protection Devices," incorporated herein by reference and copending provisional U.S. Patent Application serial number 60/489,044, filed July 22, 2003 to Ogle et al., entitled "Embolism Protection Device," incorporated herein by reference. Other specific medical devices of particular interest are described further below.

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At page 11, line 26 to page 12, line 6, please replace the paragraph with the following.

As used herein, SCF fibers refer broadly to fibers having channels or capillaries along the surface running generally along the length of the fiber or a portion thereof. Fibers have their usual meaning as structures with a length that is significantly larger than the dimensions along a cross section perpendicular to the length. The capillaries can run along substantially the entire length or a fraction thereof. Due to the presence of the capillaries, a cross section through the fiber at the capillary(ies) has a shape with an edge having changing curvatures. A suitable cross sectional shape is shown schematically in Fig. 1A, although any of wide range of cross sectional shapes are suitable as long as a surface capillary is formed. As shown schematically in Fig. 1A, the fiber has eight surface capillaries. For comparison, a fiber without surface capillaries is shown schematically in Fig. 1B at the same magnification as the fiber in Fig. 1A having roughly the same surface area as the fiber in Fig. 1A. The surface capillary fiber can have a surface area that is at least about a factor of 1.5 greater than a corresponding circular fiber with an equivalent diameter.

At page 21, line 26 to page 22, line 12, please replace the paragraph with the following.

Suitable thrombolytic agents include, for example, tissue-type plasminogen activator (tPA), mutated forms of tPA, such as TNK-tPA and YM866, urokinase, streptokinase, staphylokinase, and the like. In particular, tPA is a polypeptide that acts upon plasminogen to form plasmin. Plasmin breaks down fibrin, one of the main structural proteins in blood clots. [[(22,23)]] Plasmin also lyses fibrinogen, a precursor of fibrin. tPA can be produced according to the method described in U.S. Patent 4,935,368 to Ryotaro et al., entitled "Process For

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Producing Tissue Plasminogen Activator," incorporated herein by reference. An effective precursor of tPA is described in U.S. Patent 6,001,355 to Dowdle, entitled "Pro-tPA For The Treatment Of Thrombosis, Embolism And Related Conditions," incorporated herein by reference. Analogs, e.g., mutated forms, of tPA are known, for example, as are described in U.S. Patent 5,106,741 to Marotti et al., entitled "Tissue Plasminogen Activator (TPA) Analogs," PCT published application WO 93/20194 to Sato et al., entitled "TPA Analog," and PCT published application WO 02/22832 to Xia et al., entitled "A Cell Line Expressing Mutated Human Tissue-Type Plasminogen Activator, The Constructing Strategy Thereof And Methods Of Preparing Expressed Protein," all three of which are incorporated herein by reference. Elsewhere in this application including the claims, tPA refers to natural tPA, fragments thereof and analogs thereof that are effective to stimulate the formation of plasmin.

At page 22, lines 13-23, please replace the paragraph with the following.

Together with an appropriate materials design, a desirable medical device associated with tPA can be capable of destroying or shrinking emboli associated with cardiopulmonary bypass. Recent reports suggest that most of the emboli generated during cardiopulmonary bypass have a significant fibrin component. [(19, 20)] The body's primary means of degrading fibrin is via tissue plasminogen activator (tPA). tPA is currently in clinical use as a remedy for heart attack and stroke (thrombolysis, reperfusion therapy). This therapy involves delivering tPA through an intravenous line to break up and dissolve a clots in the coronary artery, thereby restoring blood flow. [(21)] tPA is of particular interest for use with medical devices described herein for providing protection against emboli or the like, based on the high specificity of tPA for clot degradation without causing systemic bleeding events.

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At page 25, lines 1-27, please replace the paragraph with the following.

For systemic administration, the therapeutic dose of tPA for a human patient can be 0.01 to 80 micro moles (70-8750 ng/ml) but is thought to be most effective at 500-1000 ng/ml. See, for example, Wu JH and Diamond SL, "Tissue plasminogen activator (tPA) inhibits plasmin degradation of fibrin. A mechanism that slows tPA-mediated fibrinolysis but does not require alpha 2-antiplasmin or leakage of intrinsic plasminogen," Journal Clinical Investigation 1995; 95(6):2483-2490. Lower doses may be effective with local delivery since the local concentration can be higher over the delivery period. An appropriate corresponding dose for local delivery can be sustained throughout the time of implant. If the dose is released too quickly, a toxic environment can ensue (>25,000 ng/ml for systemic delivery). See, for example, Hrach CJ, Johnson MW, Hassan AS, Lei B, Sieving PA and Elner VM, "Retinal toxicity of commercial intravitreal tissue plasminogen activator solution in cat eyes," Archive Ophthalmology 2000 May; 118(5): 659-63. To determine the initial loading dose, the release kinetics of tPA from the device can be used to deliver a desired dose of tPA or other biologically active agent. An empirical evaluation of an appropriate dose can be estimated from in vitro studies, such as the flow loop studies described in copending U.S. Patent application serial number 10/414,909 now U.S. patent 7,303,575 to Ogle, entitled "Embolism Protection Devices," incorporated herein by reference, or from animal studies. In some embodiments, it may be desirable to deliver the biologically active agent with a suitable biocompatible carrier. Suitable biocompatible carriers can be, for example, a physiologically buffered saline. Suitable buffers can be based on, for example, the following compounds: phosphate, borate, bicarbonate, carbonate, cacodylate, citrate, and other organic buffers such as tris(hydroxymethyl)aminomethane (TRIS), N-(2-hydroxyethyl) piperazine-N'-(2-ethanesulfonic acid) (HEPES) or morpholine propanesulphonic acid (MOPS). The ionic strength of the biocompatible carrier can be adjusted by the addition of

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one or more inert salts including, for example, NaCl, KCl and combinations thereof. In some embodiments, the ionic strength is near physiological values.

At page 35, line 19 to page 36, line 2, please replace the paragraph with the following.

Embolic protection devices are used to prevent the incidence of ischemic adverse events associated with embolus in vascular vessels occluding oxygenated blood to distal organs or tissues. Embolic protection devices (EPD) are described in copending U.S. Patent Application serial number 10/414,909 now U.S. patent 7,303,575 to Ogle, entitled "Embolism Protection Devices," incorporated herein by reference and copending provisional U.S. Patent Application serial number 60/489,044, filed July 22, 2003 to Ogle et al., entitled "Embolism Protection Device," incorporated herein by reference. In relation to present embodiments, the embolism protection device comprises biocompatible polymer SCF fibers. With appropriate designs, Embolic Protection Devices (EPD) incorporating SCF fibers can have two desirable properties. First, the devices with the fibers are able to conform to the complex and often asymmetrical contours of the vessel wall, thus avoiding open sites for escape of small-diameter emboli. Second, these devices can be particularly effective as a means of emboli disposal. Upon device removal, emboli are likely lodged in the device, to reduce the chance of the emboli reentering the circulation.

At page 40, lines 1-14, please replace the paragraph with the following.

With the increase in performing more complex and anatomically smaller procedures, the advent of small biological catheters is required. Yet, catheters of very small size suffer from issues of thrombosis and occlusion. The embodiment envisioned here would provide for a small catheter with an internal SCF associated surface. The presence of the surface capillaries can facilitate flow to reduce thrombosis. In addition or alternatively, the SCF fibers can be

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associated with anti-coagulation agents and/or thrombolic agents. For example, the addition of heparin sulfate surface treatment to help provide for sustained flow of blood through a small catheter. The SCF fibers can be associated with the inner surface and/or the outer surface of the catheter, for example, with an adhesive or with chemical bonding, such as crosslinking. Referring to Fig. 8A, a micro-catheter [[240]] 280 is shown schematically. Referring to Fig. 8B, a further expanded view cross sectional view of microcatheter [[240]] 280 is shown with SCF fibers [[242]] 282 along the inner surface. The size of the catheter can be selected by a person of ordinary skill in the art based on the selected use.